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=> d his

     (FILE 'HOME' ENTERED AT 14:49:03 ON 29 FEB 2008)

     FILE 'HCAPLUS' ENTERED AT 14:52:46 ON 29 FEB 2008
                E US20040259832/PN 25
L1             1 S E3

     FILE 'STNGUIDE' ENTERED AT 14:54:13 ON 29 FEB 2008

     FILE 'REGISTRY' ENTERED AT 14:55:35 ON 29 FEB 2008
L2            12 S 24980-41-4 OR 25248-42-4 OR 26023-30-3 OR 26063-00- OR 26100-
L3            18 S 9002-06-6 OR 4408-78-0 OR 4428-95-9 OR 59277-89-3 OR 66341-16
L4            30 S L2 OR L3

     FILE 'HCAPLUS' ENTERED AT 14:56:24 ON 29 FEB 2008
L5        315389 S L4
L6             1 S L5 AND L1

     FILE 'STNGUIDE' ENTERED AT 14:56:46 ON 29 FEB 2008

     FILE 'REGISTRY' ENTERED AT 15:01:27 ON 29 FEB 2008
L7                 STRUCTURE UPLOADED
L8             0 S L7 SSS SAM

     FILE 'STNGUIDE' ENTERED AT 15:02:06 ON 29 FEB 2008

     FILE 'REGISTRY' ENTERED AT 15:02:44 ON 29 FEB 2008
L9                 STRUCTURE UPLOADED
L10            0 S L9 SSS SAM

     FILE 'STNGUIDE' ENTERED AT 15:03:17 ON 29 FEB 2008

     FILE 'REGISTRY' ENTERED AT 15:09:09 ON 29 FEB 2008
L11                STRUCTURE UPLOADED
L12           50 S L11 SSS SAM
L13         2689 S L11 SSS FULL

     FILE 'HCAPLUS' ENTERED AT 15:10:03 ON 29 FEB 2008
L14         7333 S L13
L15         2679 S L14 AND HERPES

     FILE 'STNGUIDE' ENTERED AT 15:10:32 ON 29 FEB 2008

     FILE 'HCAPLUS' ENTERED AT 15:19:39 ON 29 FEB 2008
                E "161363-19-5"/BI,RN 25
L16           12 S E3
L17            8 S L16 AND L15

=> d l17 ibib abs hitstr 1-8

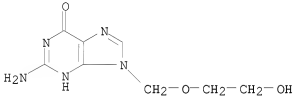
L17  ANSWER 1 OF 8  HCAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2007:636814  HCAPLUS
DOCUMENT NUMBER:          147:203162
TITLE:                    Sensitivity of monkey B virus (Cercopithecine
                          herpesvirus 1) to antiviral drugs: role of thymidine
                          kinase in antiviral activities of substrate analogs
                          and acyclonucleosides
AUTHOR(S):                Focher, Federico; Lossani, Andrea; Verri, Annalisa;
                          Spadari, Silvio; Maioli, Andrew; Gambino, Joseph J.;
                          Wright, George E.; Eberle, Richard; Black, Darla H.;
```

Medveczky, Peter; Medveczky, Maria; Shugar, David
CORPORATE SOURCE: Istituto di Genetica Molecolare, Consiglio Nazionale delle Ricerche, Pavia, 27100, Italy
SOURCE: Antimicrobial Agents and Chemotherapy (2007), 51(6), 2028-2034
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Herpes B virus (B virus [BV]) is a macaque herpesvirus that is occasionally transmitted to humans where it can cause rapidly ascending encephalitis that is often fatal. To understand the low susceptibility of BV to the acyclonucleosides, we have cloned, expressed, and characterized the BV thymidine kinase (TK), an enzyme that is expected to "activate" nucleoside analogs. This enzyme is similar in sequence and properties to the TK of herpes simplex virus (HSV), i.e., it has a broad substrate range and low enantioselectivity and is sensitive to inhibitors of HSV TKs. The BV enzyme phosphorylates some modified nucleosides and acyclonucleosides and L enantiomers of thymidine and related antiherpetic analogs. However, the potent anti-HSV drugs acyclovir (ACV), ganciclovir (GCV), and 5-bromovinyldeoxyuridine were poorly or not phosphorylated by the BV enzyme under the exptl. conditions. The antiviral activities of a number of marketed antiherpes drugs and exptl. compds. were compared against BV strains and, for comparison, HSV type 1 (HSV-1) in Vero cell cultures. For most compds. tested, BV was found to be about as sensitive as HSV-1 was. However, BV was less sensitive to ACV and GCV than HSV-1 was. The abilities of thymidine analogs and acyclonucleosides to inhibit replication of BV in Vero cell culture were not always proportional to their substrate properties for BV TK. Our studies characterize BV TK for the first time and suggest new lead compds., e.g., 5-ethyldeoxyuridine and pencyclovir, which may be superior to ACV or GCV as treatment for this emerging infectious disease.

IT 59277-89-3, Acyclovir 82410-32-0, Ganciclovir 161363-19-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monkey B virus thymidine kinase activity related to sensitivity to antiviral acyclonucleosides and thymidine analogs)

RN 59277-89-3 HCAPLUS
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)



RN 82410-32-0 HCAPLUS
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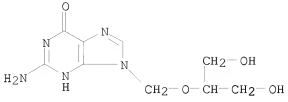

RN 161363-19-5 HCAPLUS
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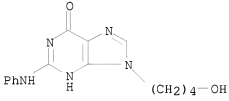
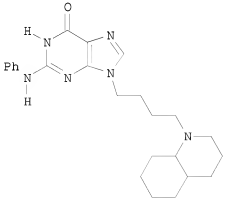


REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:398777 HCAPLUS
DOCUMENT NUMBER: 143:97319
TITLE: Inhibition of Herpes Simplex Virus Thymidine Kinases by 2-Phenylamino-6-oxopurines and Related Compounds: Structure-Activity Relationships and Antiherpetic Activity in Vivo
AUTHOR(S): Manikowski, Andrzej; Verri, Annalisa; Lossani, Andrea; Gebhardt, Bryan M.; Gambino, Joseph; Focher, Federico; Spadari, Silvio; Wright, George E.
CORPORATE SOURCE: GLSynthesis Inc., Worcester, MA, 01605, USA
SOURCE: Journal of Medicinal Chemistry (2005), 48(11), 3919-3929
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:97319
GI



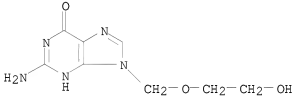
I

AB Derivs. of the herpes simplex thymidine kinase inhibitor HBPG [2-phenylamino-9-(4-hydroxybutyl)-6-oxopurine] have been synthesized and tested for inhibitory activity against recombinant enzymes (TK) from herpes simplex types 1 and 2 (HSV-1, HSV-2). The compds. inhibited phosphorylation of [3H]thymidine by both enzymes, but potencies differed quant. from those of HBPG and were generally greater for HSV-2 than HSV-1 TKs. Changes in inhibitory potency were generally consistent with the inhibitor/substrate binding site structure based on published X-ray structures of HSV-1 TK. In particular, several 9-(4-aminobutyl) analogs with bulky tertiary amino substituents were among the most potent inhibitors. Variable substrate assays showed that the most potent compound, 2-phenylamino-9-[4-(1-decahydroquinolyl)butyl]-6-oxopurine (I·2 HCl), was a competitive inhibitor, with Ki values of 0.03 and 0.005 μM against HSV-1 and HSV-2 TKs, resp. The parent compound HBPG was uniquely active in viral infection models in mice, both against ocular HSV-2 reactivation and against HSV-1 and HSV-2 encephalitis. In assays lacking [3H]thymidine, HBPG was found to be an efficient substrate for the enzymes. The ability of the TKs to phosphorylate HBPG may relate to its antiherpetic activity in vivo.

IT 59277-89-3, Acyclovir
RL: PAC (Pharmacological activity); BIOL (Biological study)
(inhibition of herpes simplex virus thymidine kinases by 2-phenylamino-6-oxopurines and related compds., structure-activity relationships and antiherpetic activity in vivo)

RN 59277-89-3 HCAPLUS

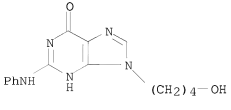
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)



IT 161363-19-5
RL: PAC (Pharmacological activity); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(inhibition of herpes simplex virus thymidine kinases by 2-phenylamino-6-oxopurines and related compds., structure-activity relationships and antiherpetic activity in vivo)

RN 161363-19-5 HCAPLUS

CN 6H-Purin-6-one, 1,9-dihydro-9-(4-hydroxybutyl)-2-(phenylamino)- (CA INDEX NAME)



IT 856669-28-8P 856669-29-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(inhibition of herpes simplex virus thymidine kinases by 2-phenylamino-6-oxopurines and related compds., structure-activity relationships and antiherpetic activity in vivo)

RN 856669-28-8 HCAPLUS
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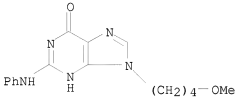

RN 856669-29-9 HCAPLUS
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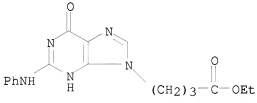


REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:681513 HCAPLUS
DOCUMENT NUMBER: 141:185078
TITLE: Novel antiherpes drug combinations of Herpes simplex virus thymidine kinase inhibitors and antiherpes substances
INVENTOR(S): Wright, George E.
PATENT ASSIGNEE(S): University of Massachusetts, USA
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

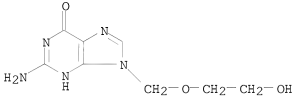
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004069168	A2	20040819	WO 2004-US2427	20040129
WO 2004069168	A3	20050915		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2514334	A1	20040819	CA 2004-2514334	20040129

US 2004259832 A1 20041223 US 2004-767019 20040129
EP 1594507 A2 20051116 EP 2004-706459 20040129
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
PRIORITY APPLN. INFO.: US 2003-443519P P 20030129
WO 2004-US2427 W 20040129

AB Composition and methods are disclosed that include a synergistic combination of an inhibitor of Herpes simplex virus thymidine kinase, and an antiherpes substance. The effect of combination of 2-phenylamino-9-(4-hydroxybutyl)-6-oxopurine and foscarnet against HSV2 encephalitis in mice was examined

IT 59277-89-3, Acyclovir 66341-16-0, Acyclovir monophosphate 82410-32-0, Ganciclovir 86761-39-9 161363-19-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiherpes drug combinations of Herpes simplex virus thymidine kinase inhibitors and antiherpes substances)

RN 59277-89-3 HCAPLUS
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)



RN 66341-16-0 HCAPLUS
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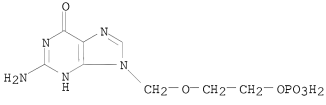

RN 82410-32-0 HCAPLUS
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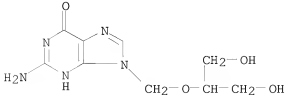

RN 86761-39-9 HCAPLUS
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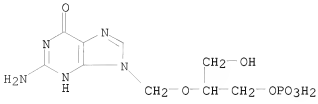
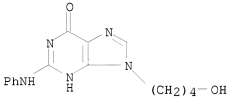
(phosphonooxy)ethoxy]methyl]- (CA INDEX NAME)



RN 161363-19-5 HCAPLUS
CN 6H-Purin-6-one, 1,9-dihydro-9-(4-hydroxybutyl)-2-(phenylamino)- (CA INDEX NAME)

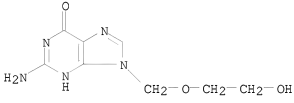


L17 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:457254 HCAPLUS
DOCUMENT NUMBER: 135:207324
TITLE: The rational of catalytic activity of herpes simplex virus thymidine kinase. A combined biochemical and quantum chemical study
AUTHOR(S): Sulpizi, Marialore; Schelling, Pierre; Folkers, Gerd; Carloni, Paolo; Scapozza, Leonardo
CORPORATE SOURCE: International School Advanced Studies, Scuola Internazionale Superiore Studi Aranzati, Trieste, 34013, Italy
SOURCE: Journal of Biological Chemistry (2001), 276(24), 21692-21697
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Most antiherpes therapies exploit the large substrate acceptance of herpes simplex virus type 1 thymidine kinase (TK HSV1) relative to the human isoenzyme. The enzyme selectively phosphosphorylates nucleoside analogs that can either inhibit viral DNA polymerase or cause toxic effects when incorporated into viral DNA. To relate structural properties of TKHSV1 ligands to their chemical reactivity we have carried out ab initio quantum chemical calcns. withing the d. functional theory framework in combination with biochem. studies. Calcns. have focused on a set of ligands carrying a representative set of the large spectrum of sugar-mimicking moieties and for which structural information of the TKHSV1ligand complex is available. The κcat values of these ligands have been measured under the same exptl. conditions using an UV spectrophotometric assay. The calcns. point to the crucial role of elec. dipole moment of ligands and its interaction with the neg. charged residue Glu225. A striking correlation is found between the energetics associated with this interaction and the κcat values measured under homogeneous conditions. This finding uncovers a fundamental aspect of the mechanism

governing substrate diversity and catalytic turnover and thus represents a significant step toward the rational design of novel and powerful prodrugs for antiviral and TKHSV1-linked suicide gene therapies.

IT 59277-89-3, Aciclovir 82410-32-0, Ganciclovir
161363-19-5
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(biochem. and quantum chemical study of nucleoside analogs interaction with herpes simplex virus thymidine kinase)

RN 59277-89-3 HCAPLUS
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)



RN 82410-32-0 HCAPLUS
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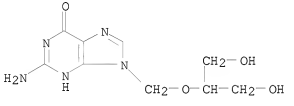

RN 161363-19-5 HCAPLUS
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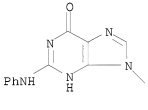
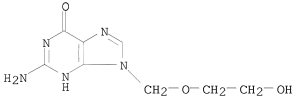


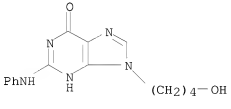
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:60517 HCAPLUS
DOCUMENT NUMBER: 130:293191
TITLE: Structure to 1.9 A resolution of a complex with herpes simplex virus type-1 thymidine kinase of a novel, non-substrate inhibitor: X-ray crystallographic comparison with binding of aciclovir
AUTHOR(S): Bennett, Matthew S.; Wien, Frank; Champness, John N.;

Batuwangala, Thilina; Rutherford, Thomas; Summers, William C.; Sun, Hongmao; Wright, George; Sanderson, Mark R.
CORPORATE SOURCE: Randall Institute, Division of Biomedical Sciences, King's College, London, WC2B 5RL, UK
SOURCE: FEBS Letters (1999), 443(2), 121-125
CODEN: FEBLAL; ISSN: 0014-5793
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Treatment of herpes infections with nucleoside analogs requires as an initial step the activation of the compds. by thymidine kinase. As an aid to developing more effective chemotherapy, both for treatment of recurrent herpes infection and in gene therapy systems where thymidine kinase is expressed, two high-resolution X-ray structures of thymidine kinase have been compared: one with the relatively poor substrate aciclovir (Zovirax), the other with a synthetic inhibitor having an N2-substituted guanine (HBPG; 9-(4-hydroxybutyl)-N2-phenylguanine). Both compds. have similar binding modes in spite of their size difference and apparently distinct ligand properties.
IT 59277-89-3D, Aciclovir, thymidine kinase complexes
161363-19-5D, thymidine kinase complexes
RL: PRP (Properties)
(crystal structure to 1.9 A resolution of a complex with herpes simplex virus type-1 thymidine kinase of a novel, non-substrate inhibitor and comparison with binding of aciclovir)
RN 59277-89-3 HCAPLUS
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[(2-hydroxyethoxy)methyl]- (CA INDEX NAME)



RN 161363-19-5 HCAPLUS
CN 6H-Purin-6-one, 1,9-dihydro-9-(4-hydroxybutyl)-2-(phenylamino)- (CA INDEX NAME)



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:456147 HCAPLUS
DOCUMENT NUMBER: 127:145171
TITLE: Phenylguanines and alkylguanines, their preparation, and their use for preventing recurrent herpes

virus infections
INVENTOR(S): Wright, George E.
PATENT ASSIGNEE(S): University of Massachusetts Medical Center, USA
SOURCE: U.S., 15 pp., Cont.-in-part of U.S. Ser. No. 241,686, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

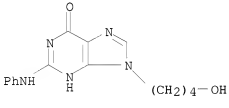
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5646155	A	19970708	US 1994-365769	19941229
WO 9620711	A1	19960711	WO 1995-US16873	19951228
W: AU, CN, JP, KR				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9646886	A	19960724	AU 1996-46886	19951228
EP 794781	A1	19970917	EP 1995-944530	19951228
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10511952	T	19981117	JP 1995-521119	19951228
PRIORITY APPLN. INFO.:			US 1994-241686	B2 19940512
			US 1994-365769	A 19941229
			WO 1995-US16873	W 19951228

OTHER SOURCE(S): MARPAT 127:145171

AB N2-substituted alkylguanines and N2-substituted phenylguanines which prevent recurrent herpes simplex infections are disclosed. By virtue of their ability to inhibit herpes virus thymidine kinase in vivo, such compds. will prevent, reduce the frequency of, or reduce the severity of recurring HSV infections in humans. Preparation of 9-(2,3-dihydroxypropyl)-N2-phenylguanine and other guanine derivs. of the invention is described, as are pharmacokinetic parameters, and effect on viral reactivation and on varicella zoster thymidine kinase.

IT 161363-19-5P
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(phenylguanine and alkylguanine preparation and use for preventing recurrent herpes virus infections)

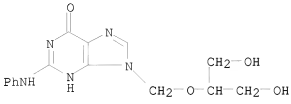
RN 161363-19-5 HCAPLUS
CN 6H-Purin-6-one, 1,9-dihydro-9-(4-hydroxybutyl)-2-(phenylamino)- (CA INDEX NAME)



IT 180867-68-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phenylguanine and alkylguanine preparation and use for preventing recurrent herpes virus infections)

RN 180867-68-9 HCAPLUS
CN 6H-Purin-6-one, 1,9-dihydro-9-[[2-hydroxy-1-(hydroxymethyl)ethoxy]methyl]-

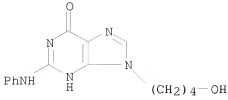
2-(phenylamino)- (CA INDEX NAME)



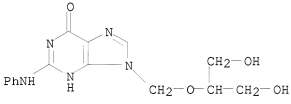
L17 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1996:548529 HCAPLUS
DOCUMENT NUMBER: 125:185858
TITLE: N2-Substituted alkylguanines and N2-substituted phenylguanines, and their preparation, to prevent recurrent herpes virus infections
INVENTOR(S): Wright, George E.
PATENT ASSIGNEE(S): University of Massachusetts Medical Center, USA
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9620711	A1	19960711	WO 1995-US16873	19951228
W: AU, CN, JP, KR				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5646155	A	19970708	US 1994-365769	19941229
AU 9646886	A	19960724	AU 1996-46886	19951228
EP 794781	A1	19970917	EP 1995-944530	19951228
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10511952	T	19981117	JP 1995-521119	19951228
PRIORITY APPLN. INFO.:			US 1994-365769 A	19941229
			US 1994-241686 B2	19940512
			WO 1995-US16873 W	19951228

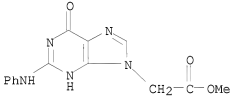
OTHER SOURCE(S): MARPAT 125:185858
AB N2-substituted alkylguanines and N2-substituted phenylguanine compds. which prevent recurrent herpes simplex infections are disclosed. By virtue of their ability to inhibit herpes virus thymidine kinase in vivo, such compds. will prevent, reduce the frequency of, or reduce the severity of recurrent HSV infections in humans. Preparation and activity of the compds. of the invention are described.
IT 161363-19-5P
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(alkylguanine and phenylguanine preparation for prevention of recurrent herpes virus infections)
RN 161363-19-5 HCAPLUS
CN 6H-Purin-6-one, 1,9-dihydro-9-(4-hydroxybutyl)-2-(phenylamino)- (CA INDEX NAME)



IT 180867-68-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alkylguanine and phenylguanine preparation for prevention of recurrent herpes virus infections)
RN 180867-68-9 HCAPLUS
CN 6H-Purin-6-one, 1,9-dihydro-9-[[2-hydroxy-1-(hydroxymethyl)ethoxy]methyl]-2-(phenylamino)- (CA INDEX NAME)



IT 180867-66-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction; alkylguanine and phenylguanine preparation for prevention of recurrent herpes virus infections)
RN 180867-66-7 HCAPLUS
CN 9H-Purine-9-acetic acid, 1,6-dihydro-6-oxo-2-(phenylamino)-, methyl ester (CA INDEX NAME)



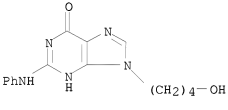
L17 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1995:283758 HCAPLUS
DOCUMENT NUMBER: 122:150822
TITLE: Synthesis, Properties, and Pharmacokinetic Studies of N2-Phenylguanine Derivatives as Inhibitors of Herpes Simplex Virus Thymidine Kinases
AUTHOR(S): Xu, Hongyan; Maga, Giovanni; Focher, Federico; Smith, Emil R.; Spadari, Silvio; Gambino, Joseph; Wright, George E.
CORPORATE SOURCE: Medical School, University of Massachusetts, Worcester, MA, 01655, USA
SOURCE: Journal of Medicinal Chemistry (1995), 38(1), 49-57
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 122:150822

AB Two series of selective inhibitors of herpes simplex virus types 1 and 2 (HSV1,2) thymidine kinases (TK) have been developed as a potential treatment for recurrent virus infections. Among compds. related to the potent base analog N2-[m-(trifluoromethyl)phenyl]guanine (mCF3PG), none was a more potent inhibitor than mCF3PG itself. Compds. related to the nucleoside N2-phenyl-2'-deoxyguanosine (PhdG), but with alkyl, hydroxyalkyl, and related substituents at the 9-position in place of the glycosyl group of PhdG, retained significant but variable inhibitory potencies against the HSV TKs. The most potent inhibitor of HSV1 TK among 9-substituted derivs., 9-(4-hydroxybutyl)-N2-phenylguanine (HBPG), was a competitive inhibitor with respect to the substrate thymidine but was not itself a substrate for the enzyme. Water solubilities and 1-octanol:water partition coeffs. for the 9-substituted N2-phenylguanines were linearly but oppositely related to the sum of hydrophobic fragmental consts. (Σf) of the 9-substituents. Four of the inhibitors were given as solns. to mice by i.v. and i.p. routes, and the time course of their plasma concns. was determined by HPLC anal. of the parent compds. HBPG was completely absorbed by the i.p. route, and the plasma concentration could be prolonged by use of suspension formulations. HBPG is a candidate for animal trials as a treatment for recurrent herpes virus infections.

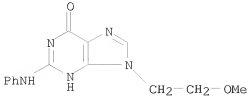
IT 161363-19-5P
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(synthesis, properties, and pharmacokinetic studies of N2-phenylguanine derivs. as inhibitors of herpes simplex virus thymidine kinases)

RN 161363-19-5 HCAPLUS
CN 6H-Purin-6-one, 1,9-dihydro-9-(4-hydroxybutyl)-2-(phenylamino)- (CA INDEX NAME)



IT 161363-22-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis, properties, and pharmacokinetic studies of N2-phenylguanine derivs. as inhibitors of herpes simplex virus thymidine kinases)

RN 161363-22-0 HCAPLUS
CN 6H-Purin-6-one, 1,9-dihydro-9-(2-methoxyethyl)-2-(phenylamino)- (CA INDEX NAME)



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